

Application No. 09/693,558

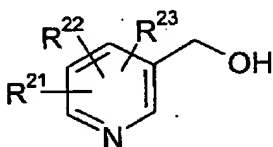
Page 2

AMENDMENT TO THE CLAIMS

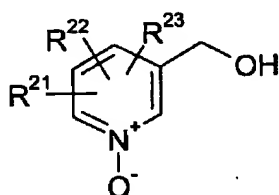
Claims 1-31 (cancelled)

32. (Currently amended): A method for ~~preventing, reducing, or eliminating~~ side effects or neutralizing the side effects of a cancerostatic or immunosuppressive agent administered prophylactically or therapeutically to a patient, comprising administering to the patient a compound having vitamin PP activity or a prodrug thereof.

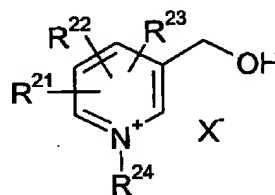
33. (Previously presented): The method of claim 32 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of compounds of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va, and Vb:



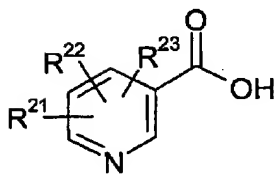
(II)



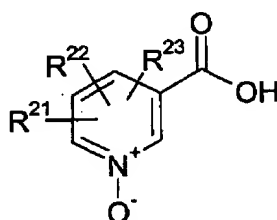
(IIa)



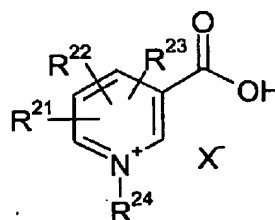
(IIb)



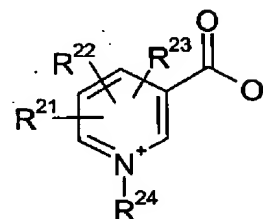
(III)



(IIIa)



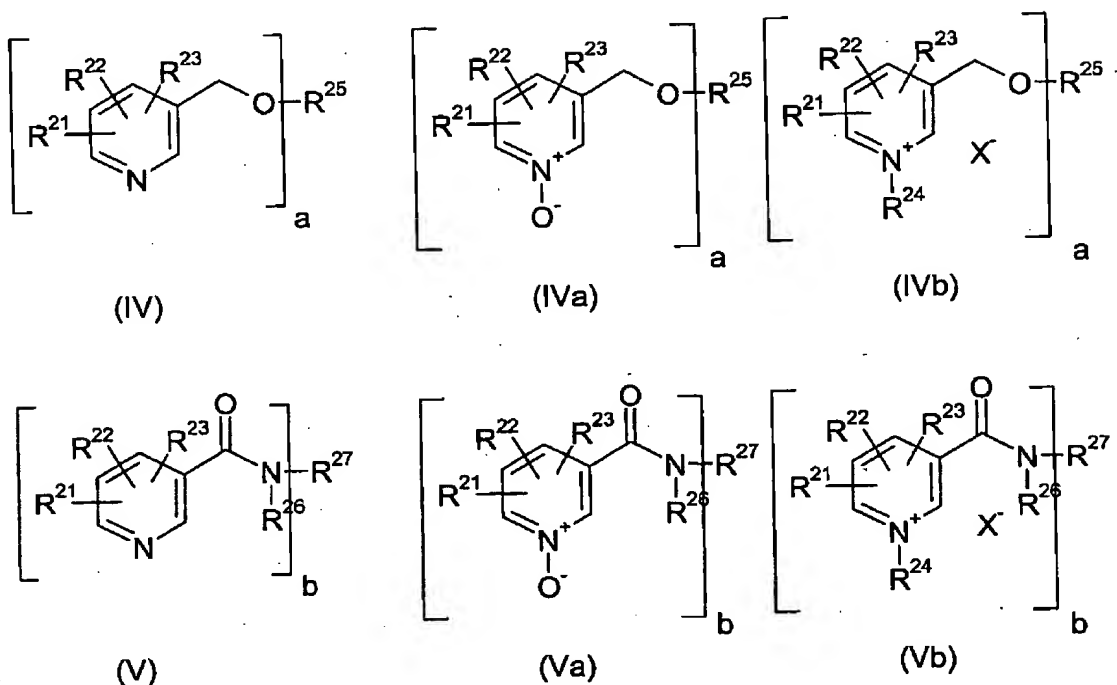
(IIIb)



(IIIc)

Application No. 09/693,558

Page 3



where:

a is an integer of 1 through 6;

b is an integer of 1 through 2;

X^- is selected from the group consisting of fluoride, chloride, bromide, iodide, hydrogensulfate, mesylate, trifluoromethanesulfonate, tosylate, tetrafluoroborate, dihydrogenphosphate, and acetate;

R^{21} is selected from the group consisting of hydrogen, halogen, cyano, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, alkylthio, aminoalkyl, amino, alkylamino, dialkylamino, formyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and carboxy;

R^{22} is selected from the group consisting of hydrogen, halogen, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, aminoalkyl, amino, alkoxycarbonyl, aminocarbonyl, and carboxy;

R^{23} is selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl;

R^{24} is selected from the group consisting of alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, and aralkyl;

Application No. 09/693,558

Page 4

R^{25} is the residue of an alcohol $R^{25}(OH)_a$ selected from monovalent linear and branched C_{1-10} alkanols and ω -dialkylaminoalkanols, benzyl alcohol, divalent linear and branched C_{2-10} diols, mono- or divalent C_{5-7} cycloalkanols, C_{5-7} cycloalkanediols, C_{5-7} cycloalkanemethanols, saturated C_{5-7} heterocyclomethanols, tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms, glycerin, 2,2-bis(hydroxymethyl)-1-octanol, erythritol, pentaerythritol, arabitol, xylitol, sorbitol, mannitol, isosorbitol, tetra(hydroxymethyl)cyclohexanol, and inositol;

R^{26} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 2, R^{27} is alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl;

and the C=S analogs of C=O groups,

and the pharmaceutical acceptable salts thereof.

34. (Previously presented): The method of claim 33 where:

R^{21} is selected from the group consisting of hydrogen, halogen, cyano, C_{1-6} alkyl, trifluoromethyl, C_{1-6} hydroxyalkyl, hydroxy, C_{1-6} alkoxy, C_{2-7} alkanoyloxy, C_{1-6} alkylthio, C_{1-6} aminoalkyl, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, formyl, alkoxycarbonyl, aminocarbonyl, (C_{1-6} alkyl)aminocarbonyl, di(C_{1-6} alkyl)aminocarbonyl, and carboxy;

R^{22} is selected from the group consisting of hydrogen, halogen, C_{1-6} alkyl, trifluoromethyl, C_{1-6} hydroxyalkyl, hydroxy, alkoxy, C_{2-7} alkanoyloxy, C_{1-6} aminoalkyl, amino, (C_{1-6} alkoxy)carbonyl, aminocarbonyl, and carboxy;

R^{23} is selected from the group consisting of hydrogen, C_{1-6} alkyl, and C_{1-6} hydroxyalkyl;

R^{24} is selected from the group consisting of C_{1-6} alkyl, C_{3-6} alkenyl, C_{2-6} hydroxyalkyl, C_{2-6} alkoxyalkyl, and benzyl;

R^{26} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, C_{3-6} alkoxyalkyl, C_{1-6} aminoalkyl, C_{4-12} dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, C_{3-6} alkoxyalkyl, C_{1-6} aminoalkyl, C_{4-12} dialkylaminoalkyl, and carboxymethyl;

Application No. 09/693,558

Page 5

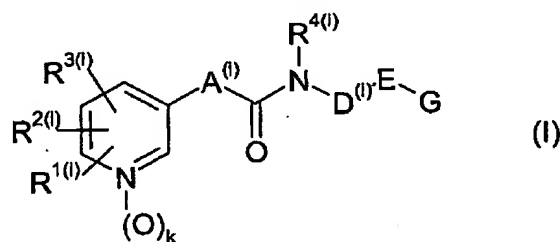
when b is 2, R^{27} is C_{2-10} alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl.

35. (Previously presented): The method of claim 34 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of nicotinic acid, nicotinamide, and their pharmaceutically acceptable ester and amide derivatives, pharmaceutical acceptable salts, quaternary, and addition salts, N-oxides, and their C=S derivatives, their isomers, and prodrugs thereof.

36. (Previously presented): The method of claim 35 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of nicotinic acid, nicotinamide, and mixtures thereof.

37. (Withdrawn): The method of claim 32 where the compound having vitamin PP activity or a prodrug thereof is tryptophan.

38. (Withdrawn): The method of claim 32 where the cancerostatic or immunosuppressive agent is selected from the group consisting of compounds of formula I:



where:

each of $R^{1(i)}$, $R^{2(i)}$, $R^{3(i)}$, and $R^{4(i)}$ are independently selected from the group consisting of hydrogen, halogen, hydroxy, trifluoromethyl, cyano, aliphatic hydrocarbyl residue optionally substituted with one or more functional groups and optionally interrupted by one or more heteroatoms, and aromatic hydrocarbyl residue; or $R^{1(i)}$ and $R^{2(i)}$ together form a bridge;

k is 0 or 1;

$A^{(i)}$ and $D^{(i)}$ are independently a saturated or unsaturated optionally substituted aliphatic hydrocarbyl residue, optionally interrupted by a heteroatom or a functional group;

Application No. 09/693,558

Page 6

E is a bond or is a heterocyclic residue having one or two ring nitrogen atoms or one ring nitrogen atom and one ring oxygen atom, linked to D⁽ⁱ⁾ and G through a ring nitrogen atom and a ring carbon atom or through two ring nitrogen atoms; and

G is selected from the group consisting of hydrogen, an aliphatic or araliphatic residue, an unsaturated or aromatic monocyclic or polycyclic carbocyclic residue, a saturated, unsaturated, or aromatic monocyclic or polycyclic heterocyclic residue, bonded directly or through a functional group derived from a carbon, nitrogen, oxygen, sulfur, or phosphorus atom,

and the stereoisomers or racemic or non-racemic mixtures of stereoisomers thereof,

and the tautomers thereof when G is a heterocyclic aromatic ring or an aromatic ring substituted by a hydroxy, mercapto, or amino group,

and the pharmacologically acceptable acid addition salts thereof.

39. (Withdrawn): The method of claim 50 where the cancerostatic or immunosuppressive agent is selected from the group consisting of

N-[2-(1-benzylpiperidin-4-yl)ethyl]-3-(pyridin-3-yl)propionamide;

N-{2-[1-(2-phenylethyl)piperidin-4-yl]ethyl}-3-(pyridin-3-yl)-propionamide;

N-{2-[1-(4-phenylbutyl)piperidin-4-yl]ethyl}-3-(pyridin-3-yl)-propionamide;

N-{2-[1-(4-hydroxy-4-phenylbutyl)piperidin-4-yl]ethyl}-3-(pyridin-3-yl)propionamide;

N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-3-(pyridin-3-yl)-propionamide;

N-[3-(1-diphenylmethylpiperidin-4-yl)propyl]-3-(pyridin-3-yl)propionamide;

N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;

N-[4-(1-benzylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;

N-{4-[1-(2-phenylethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)-acrylamide;

N-{4-[1-(4-biphenylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;

N-{4-[1-(1-naphthylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;

N-{4-[1-(9-anthrylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;

N-{4-[1-(cyclohexylphenylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;

N-{4-[1-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)-acrylamide;

N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-3-(pyridin-3-yl)acrylamide;

N-[3-(1-diphenylmethylpiperidin-4-yl)propyl]-3-(pyridin-3-yl)acrylamide;

Application No. 09/693,558

Page 7

N-[5-(1-diphenylmethylpiperidin-4-yl)pentyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(1-diphenylmethylpiperidin-4-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-(4-{1-[bis(4-fluorophenyl)methyl]piperidin-4-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-(4-{1-[bis(2-chlorophenyl)methyl]piperidin-4-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(2-fluoro-pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(6-fluoro-pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide dihydrochloride;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide methanesulfonate;
N-[4-(1-acetylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-benzoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylacetylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-{4-[1-(9-oxo-9H-fluoren-4-carbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-methylsulfonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-{4-[1-(2-naphthylsulfonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-benzylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-(4-{1-[bis(2-chlorophenyl)methyl]piperidin-4-yl}butyl)-3-(pyridin-3-yl)propionamide;
N-{4-[1-(phenylpyridin-3-ylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[1-(9H-fluoren-9-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)piperidin-4-yl]-butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[1-(1-naphthylaminocarbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylaminocarbonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-{4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)-propionamide;
N-[4-(1-diphenylphosphinoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(2-fluoropyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(5-fluoropyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-2-fluoro-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-2,2-difluoro-3-(pyridin-3-yl)propionamide;

Application No. 09/693,558

Page 8

N-[5-(1-diphenylmethylpiperidin-4-yl)pentyl]-3-(pyridin-3-yl)propionamide;
N-[6-(1-diphenylmethylpiperidin-4-yl)hexyl]-3-(pyridin-3-yl)propionamide;
N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-5-(pyridin-3-yl)pentanoic acid amide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)pentanoic acid amide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-N-hydroxy-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-2-hydroxy-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-hydroxy-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-methylsulfonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(2-naphthylsulfonyl)piperidin-4-yl]butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(2-naphthylsulfonyl)piperidin-4-yl]butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-[1-(1-naphthylaminocarbonyl)piperidin-4-yl]butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylaminocarbonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylaminocarbonylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)piperidin-4-yl]-butyl]-3-(pyridin-3-yl)-acrylamide;
N-[4-(1-diphenylphosphinoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-acetylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylacetylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(3,3-diphenylpropionyl)piperidin-4-yl]-butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-benzoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-benzoylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-[1-(9-oxo-9H-fluoren-4-ylcarbonyl)piperidin-4-yl]butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(phenylpyridin-3-ylmethyl)piperidin-4-yl]-butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(phenylpyridin-4-ylmethyl)piperidin-4-yl]-butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)piperidin-4-yl]butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-[1-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)piperidin-4-yl]-butyl]-3-(pyridin-3-yl)acrylamide;
N-[7-(1-diphenylmethylpiperidin-4-yl)heptyl]-3-(pyridin-3-yl)acrylamide;
N-[8-(1-diphenylmethylpiperidin-4-yl)octyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(1-diphenylmethylpiperidin-4-yloxy)propyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(1-benzylpiperidin-4-yloxy)propyl]-3-(pyridin-3-yl)acrylamide;

Application No. 09/693,558

Page 9

N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[5-(1-diphenylmethylpiperidin-4-yl)pentyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[6-(1-diphenylmethylpiperidin-4-yl)hexyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-(4-diphenylmethylpiperazin-1-yl)-3-hydroxybutyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(4-diphenylmethylpiperazin-1-yl)propoxy]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylmethylpiperazin-1-yl)-4-oxobutyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(4-diphenylmethylpiperazin-1-sulfonyl)propyl]-3-(pyridin-3-yl)acrylamide;
N-{2-[2-(4-diphenylmethylpiperazin-1-yl)ethoxy]ethyl}-3-(pyridin-3-yl)acrylamide;
N-(4-{4-[bis(4-fluorophenyl)methyl]piperazin-1-yl}but-2-enyl)-3-(pyridin-3-yl)acrylamide;
N-(4-{4-[(4-carboxyphenyl)phenylmethyl]piperazin-1-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-(4-{4-[(4-aminophenyl)phenylmethyl]piperazin-1-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(9H-fluoren-9-yl)piperazin-1-yl]butyl}-2-(pyridin-3-yloxy)acetamide;
N-{5-[4-(9H-fluoren-9-yl)piperazin-1-yl]pentyl}-3-(pyridin-3-yl)acrylamide;
N-{6-[4-(9H-fluoren-9-yl)piperazin-1-yl]hexyl}-3-(pyridin-3-yl)acrylamide;
3-(pyridin-3-yl)-N-{4-[4-(1,2,3,4-tetrahydronaphthalen-1-yl)piperazin-1-yl]butyl}acrylamide;
3-(pyridin-3-yl)-N-{4-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]butyl}acrylamide;
N-{4-[4-(naphthalen-1-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[5-(4-biphenyl-2-ylpiperazin-1-yl)pentyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(4-biphenyl-2-ylpiperazin-1-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-2-(pyridin-3-yloxy)acetamide;
N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-{4-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)-propionamide;
N-{5-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]pentyl}-3-(pyridin-3-yl)-acrylamide;
N-{6-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]hexyl}-3-(pyridin-3-yl)-acrylamide;
N-{4-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]butyl}-5-(pyridin-3-yl)-2,4-pentadienic amide;

Application No. 09/693,558

Page 10

N-{4-[4-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{2-[4-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)piperazin-1-yl]ethyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylacetyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-benzoylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(2-aminobenzoyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(4-carboxybenzoyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(biphenyl-2-carbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(9-oxo-9H-fluoren-4-carbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(furan-2-carbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(naphthalen-1-ylaminocarbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[4-(diphenylaminocarbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(naphthalen-2-sulfonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylphosphinonylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-biphenyl-2-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(9H-fluoren-9-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)-
acrylamide;
N-[4-(4-phenylpiperidin-1-yl)-butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(1H-indol-3-yl)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(2-oxo-2,3-dihydrobenzimidazol-1-yl)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-benzotriazol-1-yl)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(hydroxydiphenylmethyl)piperidin-1-yl]butyl}-2-(pyridin-3-yloxy)acetamide;
N-[4-(4,4-diphenylpiperidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(6,11-dihydrodibenzo[b,e]thiepin-11-yliden)piperidin-1-yl]butyl}-3-(pyridin-3-
yl)propionamide dihydrochloride semi-isopropanol;
N-{4-[4-(6,11-dihydrodibenzo[b,e]thiepin-11-yliden)piperidin-1-yl]butyl}-5-(pyridin-3-
yl)pentanamide;
N-{4-[4-(4,9-dihydrothieno[2,3-b]benzo[e]thiepin-4-yliden)piperidin-1-yl]butyl}-3-(pyridin-3-yl)-
propionamide;
N-{4-[4-(4,9-dihydrothieno[2,3-b]benzo[e]thiepin-4-yliden)piperidin-1-yl]butyl}-3-(pyridin-3-yl)-
acrylamide;

Application No. 09/693,558

Page 11

N-[4-(4-diphenylphosphinoyloxypiperidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,4-dioxo-8-azaspiro[4.5]dec-8-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,6-dioxo-4-phenylpiperidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3-dioxo-4,5,6,7-tetraphenyl-1,3-dihydroisoindol-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(3-benzyl-2,4,5-trioxoimidazolidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3,10-trioxo-1,4,5,6,10,10a-hexahydroacenaphtho[1,8a-c]pyrrol-2-yl)butyl]-3-(pyridin-3-yl)-
acrylamide;
N-[4-(2,5-dioxo-4,4-diphenylimidazolidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-3-phenyl-2,5-dihydropyrrol-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)propyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(3-pyridin-3-ylacryloylamino)butyl]-2,3:5,6-dibenzobicyclo[2.2.2]octan-7,8-dicarboximide;
N-[4-(5-benzyliden-2,4-dioxothiazolidin-3-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-benzyl-2,6-dioxopiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1,3-dioxo-1,3-dihydroisoindol-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)butyl]-3-(1-oxopyridin-3-yl)acrylamide;
N-[6-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[2-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)ethyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[8,8-bis(4-fluorophenyl)octyl]-3-(pyridin-3-yl)acrylamide hydrochloride;
N-[6-(3,3-diphenylureido)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-phenyl-1,2,4,5-tetrahydrobenzo[d]azepin-3-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-(8,8-diphenyloctyl)-3-(pyridin-3-yl)acrylamide;
N-(8-hydroxy-8,8-diphenyloctyl)-3-(pyridin-3-yl)acrylamide;
N-[4-(3,3-diphenylureido)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1H,3H-benzo[de]isoquinolin-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(10,11-dihydrodibenzo[b,f]azepin-5-ylcarbonylamino)hexyl]-3-(pyridin-3-yl)acrylamide;
3-(pyridin-3-yl)-N-[6-tosylaminohexyl]acrylamide;
N-[4-(1,1-dioxo-1-thia-2-azaacenaphthylen-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;

Application No. 09/693,558

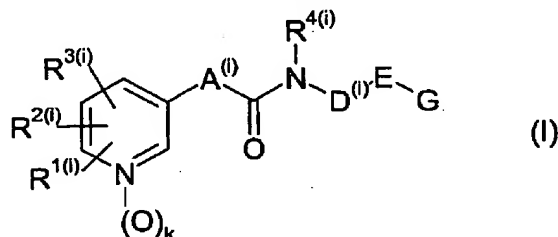
Page 12

N-(6-hydroxy-6,6-diphenylhexyl)-3-(pyridin-3-yl)acrylamide;
 N-(6,6-diphenylhex-5-enyl)-3-(pyridin-3-yl)acrylamide;
 N-[4-(4,5-diphenylimidazol-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
 N-[4-(trans-2-phenylcyclopropylcarbonylamino)butyl]-3-(pyridin-3-yl)acrylamide;
 N-(5-hydroxy-5,5-diphenylpentyl)-3-(pyridin-3-yl)acrylamide;
 N-(7-phenylheptyl)-3-(pyridin-3-yl)acrylamide;
 N-(4-diphenylacetylaminobutyl)-3-(pyridin-3-yl)acrylamide;
 N-[4-(benzhydrylamino)butyl]-3-(pyridin-3-yl)acrylamide; and
 N-[4-[[2-(benzhydrylmethylamino)ethyl]methylamino]butyl]-3-(pyridin-3-yl)acrylamide.

40. (Withdrawn): The method of claim 50 comprising the additional administration of a further cancerostatic or immunosuppressive agent that is not a compound of formula Ia.

41. (Withdrawn): A pharmaceutical composition comprising:

(a) at least one compound selected from the group consisting of compounds of formula I:



where:

each of $R^{1(i)}$, $R^{2(i)}$, $R^{3(i)}$, and $R^{4(i)}$ are independently selected from the group consisting of hydrogen, halogen, hydroxy, trifluoromethyl, cyano, aliphatic hydrocarbyl residue optionally substituted with one or more functional groups and optionally interrupted by one or more heteroatoms, and aromatic hydrocarbyl residue; or $R^{1(i)}$ and $R^{2(i)}$ together form a bridge;

k is 0 or 1;

$A^{(i)}$ and $D^{(i)}$ are independently a saturated or unsaturated optionally substituted aliphatic hydrocarbyl residue, optionally interrupted by a heteroatom or a functional group;

E is a bond or is a heterocyclic residue having one or two ring nitrogen atoms or one ring nitrogen atom and one ring oxygen atom, linked to $D^{(i)}$ and G through a ring nitrogen atom and a ring carbon atom or through two ring nitrogen atoms; and

Application No. 09/693,558

Page 13

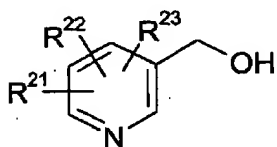
G is selected from the group consisting of hydrogen, an aliphatic or araliphatic residue, an unsaturated or aromatic monocyclic or polycyclic carbocyclic residue, a saturated, unsaturated, or aromatic monocyclic or polycyclic heterocyclic residue, bonded directly or through a functional group derived from a carbon, nitrogen, oxygen, sulfur, or phosphorus atom,

and the stereoisomers or racemic or non-racemic mixtures of stereoisomers thereof,

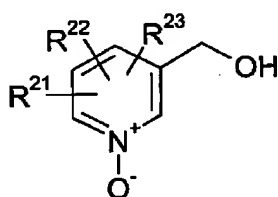
and the tautomers thereof when G is a heterocyclic aromatic ring or an aromatic ring substituted by a hydroxy, mercapto, or amino group,

and the pharmacologically acceptable acid addition salts thereof;

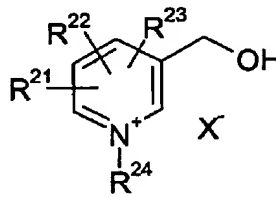
(b) at least one compound selected from the group consisting of compounds of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va, and Vb:



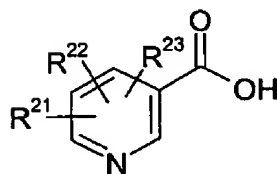
(II)



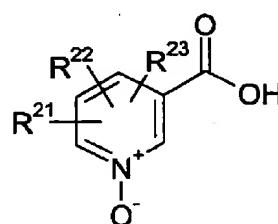
(IIa)



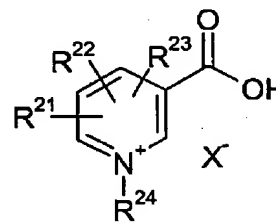
(IIb)



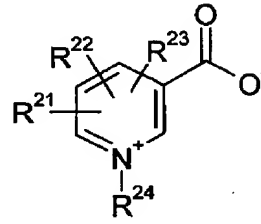
(III)



(IIIa)



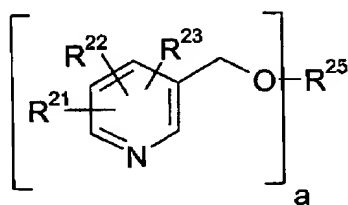
(IIIb)



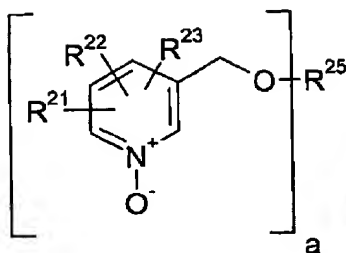
(IIIc)

Application No. 09/693,558

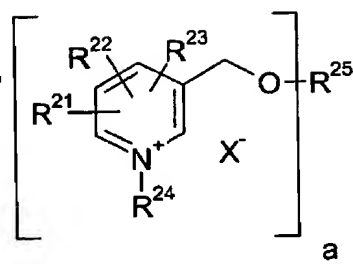
Page 14



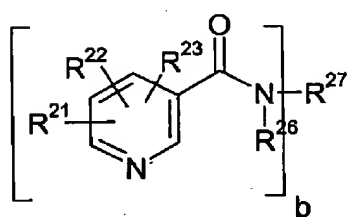
(IV)



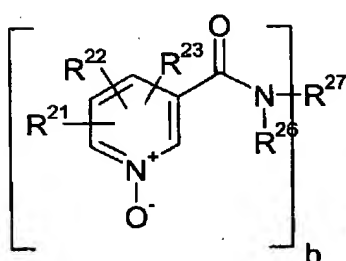
(IVa)



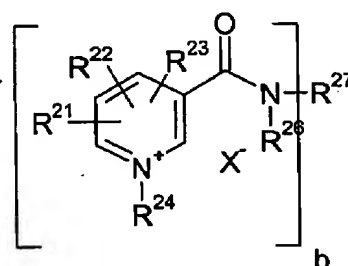
(IVb)



(V)



(Va)



(Vb)

where:

a is an integer of 1 through 6;

b is an integer of 1 through 2;

X⁻ is selected from the group consisting of fluoride, chloride, bromide, iodide, hydrogensulfate, mesylate, trifluoromethanesulfonate, tosylate, tetrafluoroborate, dihydrogenphosphate, and acetate;

R²¹ is selected from the group consisting of hydrogen, halogen, cyano, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, alkylthio, aminoalkyl, amino, alkylamino, dialkylamino, formyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and carboxy;

R²² is selected from the group consisting of hydrogen, halogen, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, aminoalkyl, amino, alkoxycarbonyl, aminocarbonyl, and carboxy;

R²³ is selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl;

R²⁴ is selected from the group consisting of alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, and aralkyl;

Application No. 09/693,558

Page 15

R^{25} is the residue of an alcohol $R^{25}(OH)_a$ is selected from monovalent linear and branched C_{1-10} alkanols and ω -dialkylaminoalkanols, benzyl alcohol, divalent linear and branched C_{2-10} diols, mono- or divalent C_{5-7} cycloalkanols, C_{5-7} cycloalkanediols, C_{5-7} cycloalkanemethanols, saturated C_{5-7} heterocyclomethanols, tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms, glycerin, 2,2-bis(hydroxymethyl)-1-octanol, erythritol, pentaerythritol, arabitol, xylitol, sorbitol, mannitol, isosorbitol, tetra(hydroxymethyl)cyclohexanol, and inositol;

R^{26} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 2, R^{27} is alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl;

and the C=S analogs of C=O groups,

and the pharmaceutical acceptable salts thereof; and

(c) at least one physiologically acceptable carrier.

42. (Withdrawn): The composition of claim 52 comprising a further cancerostatic or immunosuppressive agent that is not a compound of formula I.

43. (Withdrawn): The composition of claim 52 where the compound(s) of formula Ia and the compound(s) of formula II - Vb are contained separately within the composition.

44. (Withdrawn): The composition of claim 52 where the compound(s) of formula Ia and the compound(s) of formula II - Vb are present in separate dosage forms, and the dosage forms are packaged together for co-administration.

45. (Withdrawn) The composition of claim 52 where:

R^{21} is selected from the group consisting of hydrogen, halogen, cyano, C_{1-6} alkyl, trifluoromethyl, C_{1-6} hydroxyalkyl, hydroxy, C_{1-6} alkoxy, C_{2-7} alkanoyloxy, C_{1-6} alkylthio, C_{1-6} aminoalkyl, amino, C_{1-6} alkylamino, di(C_{1-6} alkyl)amino, formyl, alkoxy carbonyl, aminocarbonyl, (C_{1-6} alkyl)aminocarbonyl, di(C_{1-6} alkyl)aminocarbonyl, and carboxy;

Application No. 09/693,558

Page 16

R²² is selected from the group consisting of hydrogen, halogen, C₁₋₆ alkyl, trifluoromethyl, C₁₋₆ hydroxyalkyl, hydroxy, alkoxy, C₂₋₇ alkanoyloxy, C₁₋₆ aminoalkyl, amino, (C₁₋₆ alkoxy)carbonyl, aminocarbonyl, and carboxy;

R²³ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, and C₁₋₆ hydroxyalkyl;

R²⁴ is selected from the group consisting of C₁₋₆ alkyl, C₃₋₆ alkenyl, C₂₋₆ hydroxyalkyl, C₂₋₆ alkoxyalkyl, and benzyl;

R²⁶ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, C₃₋₆ alkoxyalkyl, C₁₋₆ aminoalkyl, C₄₋₁₂ dialkylaminoalkyl, and carboxymethyl;

when b is 1, R²⁷ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ hydroxyalkyl, C₃₋₆ alkoxyalkyl, C₁₋₆ aminoalkyl, C₄₋₁₂ dialkylaminoalkyl, and carboxymethyl; and

when b is 2, R²⁷ is C₂₋₁₀ alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl.

46. (Withdrawn): The composition of claim 52 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of nicotinic acid, nicotinamide, and their pharmaceutically acceptable ester and amide derivatives, pharmaceutical acceptable salts, quaternary, and addition salts, N-oxides, and their C=S derivatives, their isomers, and prodrugs thereof.

47. (Withdrawn): The composition of claim 46 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of nicotinic acid, nicotinamide, and mixtures thereof.

48. (Withdrawn): The composition of claim 51 where the compound having vitamin PP activity or a prodrug thereof is tryptophan.

49. (Withdrawn): The composition of claim 52 where the compound(s) of formula Ia are selected from the group consisting of

N-[2-(1-benzylpiperidin-4-yl)ethyl]-3-(pyridin-3-yl)propionamide;

N-{2-[1-(2-phenylethyl)piperidin-4-yl]ethyl}-3-(pyridin-3-yl)propionamide;

N-{2-[1-(4-phenylbutyl)piperidin-4-yl]ethyl}-3-(pyridin-3-yl)propionamide;

N-{2-[1-(4-hydroxy-4-phenylbutyl)piperidin-4-yl]ethyl}-3-(pyridin-3-yl)propionamide;

Application No. 09/693,558

Page 17

N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-3-(pyridin-3-yl)propionamide,
N-[3-(1-diphenylmethylpiperidin-4-yl)propyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-benzylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(2-phenylethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(4-biphenylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(1-naphthylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)-acrylamide;
N-{4-[1-(9-anthrylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(cyclohexylphenylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)-
acrylamide;
N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(1-diphenylmethylpiperidin-4-yl)propyl]-3-(pyridin-3-yl)acrylamide;
N-[5-(1-diphenylmethylpiperidin-4-yl)pentyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(1-diphenylmethylpiperidin-4-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-(4-{1-[bis(4-fluorophenyl)methyl]piperidin-4-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-(4-{1-[bis(2-chlorophenyl)methyl]piperidin-4-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(2-fluoro-pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(6-fluoro-pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide dihydrochloride;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide methanesulfonate;
N-[4-(1-acetyl piperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-benzoyl piperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylacetyl piperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-{4-[1-(9-oxo-9H-fluoren-4-carbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-methylsulfonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-{4-[1-(2-naphthylsulfonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-benzyl piperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-(4-{1-[bis(2-chlorophenyl)methyl]piperidin-4-yl}butyl)-3-(pyridin-3-yl)propionamide;

Application No. 09/693,558

Page 18

N-{4-[1-(phenylpyridin-3-ylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[1-(9H-fluoren-9-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[1-(1-naphthylaminocarbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylaminocarbonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-{4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylphosphinoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(2-fluoropyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(5-fluoropyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-2-fluoro-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-2,2-difluoro-3-(pyridin-3-yl)propionamide;
N-[5-(1-diphenylmethylpiperidin-4-yl)pentyl]-3-(pyridin-3-yl)propionamide;
N-[6-(1-diphenylmethylpiperidin-4-yl)hexyl]-3-(pyridin-3-yl)propionamide;
N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-5-(pyridin-3-yl)pentanoic acid amide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)pentanoic acid amide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-N-hydroxy-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-2-hydroxy-3-(pyridin-3-yl)propionamide;
N-{4-(1-diphenylmethylpiperidin-4-yl)butyl}-3-hydroxy-3-(pyridin-3-yl)propionamide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1-methylsulfonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(2-naphthylsulfonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(2-naphthylsulfonyl)piperidin-4-yl]butyl}-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-{4-[1-(1-naphthylaminocarbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylaminocarbonylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylaminocarbonylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-{4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(1-diphenylphosphinoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-acetylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;

Application No. 09/693,558

Page 19

N-[4-(1-diphenylacetyl)piperidin-4-yl]-butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(3,3-diphenylpropionyl)piperidin-4-yl]-butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(1-benzoylpiperidin-4-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1-benzoylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-{4-[1-(9-oxo-9H-fluoren-4-ylcarbonyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(phenylpyridin-3-ylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(phenylpyridin-4-ylmethyl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[1-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)piperidin-4-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[7-(1-diphenylmethylpiperidin-4-yl)heptyl]-3-(pyridin-3-yl)acrylamide;
N-[8-(1-diphenylmethylpiperidin-4-yl)octyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(1-diphenylmethylpiperidin-4-yloxy)propyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(1-benzylpiperidin-4-yloxy)propyl]-3-(pyridin-3-yl)acrylamide;
N-[2-(1-diphenylmethylpiperidin-4-yl)ethyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-(1-diphenylmethylpiperidin-4-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[5-(1-diphenylmethylpiperidin-4-yl)pentyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[6-(1-diphenylmethylpiperidin-4-yl)hexyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-[4-(4-diphenylmethylpiperazin-1-yl)-3-hydroxybutyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(4-diphenylmethylpiperazin-1-yl)propoxy]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylmethylpiperazin-1-yl)-4-oxobutyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(4-diphenylmethylpiperazin-1-sulfonyl)propyl]-3-(pyridin-3-yl)acrylamide;
N-{2-[2-(4-diphenylmethylpiperazin-1-yl)ethoxy]ethyl}-3-(pyridin-3-yl)acrylamide;
N-(4-{4-[bis(4-fluorophenyl)methyl]piperazin-1-yl}but-2-enyl)-3-(pyridin-3-yl)acrylamide;
N-(4-{4-[(4-carboxyphenyl)phenylmethyl]piperazin-1-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-(4-{4-[(4-aminophenyl)phenylmethyl]piperazin-1-yl}butyl)-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(9H-fluoren-9-yl)piperazin-1-yl]butyl}-2-(pyridin-3-yloxy)acetamide;
N-{5-[4-(9H-fluoren-9-yl)piperazin-1-yl]pentyl}-3-(pyridin-3-yl)acrylamide;
N-{6-[4-(9H-fluoren-9-yl)piperazin-1-yl]hexyl}-3-(pyridin-3-yl)acrylamide;
3-(pyridin-3-yl)-N-{4-[4-(1,2,3,4-tetrahydronaphthalen-1-yl)piperazin-1-yl]butyl}acrylamide;
3-(pyridin-3-yl)-N-{4-[4-(5,6,7,8-tetrahydronaphthalen-1-yl)piperazin-1-yl]butyl}acrylamide;
N-{4-[4-(naphthalen-1-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;

Application No. 09/693,558

Page 20

N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[5-(4-biphenyl-2-ylpiperazin-1-yl)pentyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(4-biphenyl-2-ylpiperazin-1-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-2-(pyridin-3-yloxy)acetamide;
N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-5-(pyridin-3-yl)-2,4-pentadienic acid amide;
N-{4-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)-propionamide;
N-{5-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]pentyl}-3-(pyridin-3-yl)-acrylamide;
N-{6-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]hexyl}-3-(pyridin-3-yl)-acrylamide;
N-{4-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]butyl}-5-(pyridin-3-yl)-2,4-pentadienic amide;
N-{4-[4-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{2-[4-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)piperazin-1-yl]ethyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylacetyl)piperazin-1-yl]butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-benzoylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(2-aminobenzoyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(4-carboxybenzoyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(biphenyl-2-carbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(9-oxo-9H-fluoren-4-carbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(furan-2-carbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(naphthalen-1-ylaminocarbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[4-(diphenylaminocarbonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(naphthalen-2-sulfonyl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylphosphinonylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-biphenyl-2-ylpiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(9H-fluoren-9-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-yl)piperazin-1-yl]butyl}-3-(pyridin-3-yl)-acrylamide;
N-[4-(4-phenylpiperidin-1-yl)-butyl]-3-(pyridin-3-yl)acrylamide;

Application No. 09/693,558

Page 21

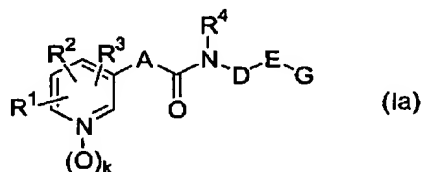
N-{4-[4-(1H-indol-3-yl)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(2-oxo-2,3-dihydrobenzimidazol-1-yl)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-benzotriazol-1-yl)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(hydroxydiphenylmethyl)piperidin-1-yl]butyl}-2-(pyridin-3-yloxy)acetamide;
N-[4-(4,4-diphenylpiperidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-{4-[4-(6,11-dihydrodibenzo[b,e]thiepin-11-yliden)piperidin-1-yl]butyl}-3-(pyridin-3-yl)propionamide dihydrochloride semi-isopropanol;
N-{4-[4-(6,11-dihydrodibenzo[b,e]thiepin-11-yliden)piperidin-1-yl]butyl}-5-(pyridin-3-yl)pentanamide;
N-{4-[4-(4,9-dihydrothieno[2,3-b]benzo[e]thiepin-4-yliden)piperidin-1-yl]butyl}-3-(pyridin-3-yl)propionamide;
N-{4-[4-(4,9-dihydrothieno[2,3-b]benzo[e]thiepin-4-yliden)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(4-diphenylphosphinoxyloxy)piperidin-1-yl]butyl}-3-(pyridin-3-yl)acrylamide;
N-[4-(1,4-dioxo-8-azaspiro[4.5]dec-8-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,6-dioxo-4-phenylpiperidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3-dioxo-4,5,6,7-tetraphenyl-1,3-dihydroisoindol-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(3-benzyl-2,4,5-trioxoimidazolidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3,10-trioxo-1,4,5,6,10,10a-hexahydroacenaphtho[1,8a-c]pyrrol-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-4,4-diphenylimidazolidin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-3-phenyl-2,5-dihydropyrrol-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[3-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)propyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(3-pyridin-3-ylacryloylamino)butyl]-2,3:5,6-dibenzobicyclo[2.2.2]octan-7,8-dicarboximide;
N-[4-(5-benzyliden-2,4-dioxothiazolidin-3-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(4-benzyl-2,6-dioxopiperazin-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[6-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(2,5-dioxo-3,4-diphenyl-2,5-dihydropyrrol-1-yl)butyl]-3-(pyridin-3-yl)propionamide;
N-[4-(1,3-dioxo-1,3-dihydroisoindol-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
N-[4-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)butyl]-3-(1-oxopyridin-3-yl)acrylamide;

Application No. 09/693,558

Page 22

N-[6-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)hexyl]-3-(pyridin-3-yl)acrylamide;
 N-[2-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)ethyl]-3-(pyridin-3-yl)acrylamide;
 N-[4-(1,3-dioxo-1H,3H-benzo[de]isoquinolin-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
 N-[8,8-bis(4-fluorophenyl)octyl]-3-(pyridin-3-yl)acrylamide hydrochloride;
 N-[6-(3,3-diphenylureido)hexyl]-3-(pyridin-3-yl)acrylamide;
 N-[4-(1-phenyl-1,2,4,5-tetrahydrobenzo[d]azepin-3-yl)butyl]-3-(pyridin-3-yl)acrylamide;
 N-(8,8-diphenyloctyl)-3-(pyridin-3-yl)acrylamide;
 N-(8-hydroxy-8,8-diphenyloctyl)-3-(pyridin-3-yl)acrylamide;
 N-[4-(3,3-diphenylureido)butyl]-3-(pyridin-3-yl)acrylamide;
 N-[4-(1H,3H-benzo[de]isoquinolin-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
 N-[6-(10,11-dihydrodibenzo[b,f]azepin-5-ylcarbonylamino)hexyl]-3-(pyridin-3-yl)acrylamide;
 3-(pyridin-3-yl)-N-[6-tosylaminoethyl]acrylamide;
 N-[4-(1,1-dioxo-1-thia-2-azaacenaphthylen-2-yl)butyl]-3-(pyridin-3-yl)acrylamide;
 N-(6-hydroxy-6,6-diphenylhexyl)-3-(pyridin-3-yl)acrylamide;
 N-(6,6-diphenylhex-5-enyl)-3-(pyridin-3-yl)acrylamide;
 N-[4-(4,5-diphenylimidazol-1-yl)butyl]-3-(pyridin-3-yl)acrylamide;
 N-[4-(trans-2-phenylcyclopropylcarbonylamino)butyl]-3-(pyridin-3-yl)acrylamide;
 N-(5-hydroxy-5,5-diphenylpentyl)-3-(pyridin-3-yl)acrylamide;
 N-(7-phenylheptyl)-3-(pyridin-3-yl)acrylamide;
 N-(4-diphenylacetylaminobutyl)-3-(pyridin-3-yl)acrylamide;
 N-[4-(benzhydrylamino)butyl]-3-(pyridin-3-yl)acrylamide; and
 N-(4-{[2-(benzhydrylmethylamino)ethyl]methylamino}butyl)-3-(pyridin-3-yl)acrylamide.

50. (Withdrawn): The method of claim 38 where the cancerostatic or immunosuppressive agent is selected from the group consisting of compounds of formula Ia:



where:

Application No. 09/693,558

Page 23

R¹ is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl, and hydroxy;

R² and R³ are each hydrogen;

R⁴ is hydrogen or hydroxy;

A is selected from the group consisting of ethylene, propylene, or butylene, each optionally substituted with hydroxy or one or two fluorine atoms, -OCH₂-, -SCH₂-, ethenylene, vinylene, and butadienylene;

D is selected from the group consisting of C₂ - C₆ alkylene and C₂ - C₆ alkenylene, where the double bond may also join D and E;

E is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine, and morpholine; and

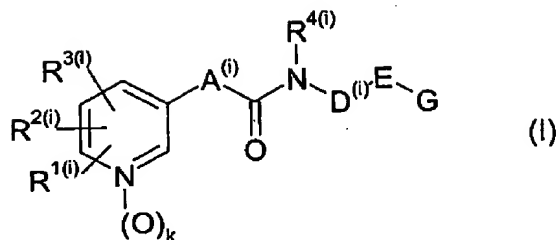
G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl, furylmethyl, thienylmethyl, thiazolylmethyl, pyridylmethyl, benzothienylmethyl, quinolylmethyl, phenylthienylmethyl, phenylpyridylmethyl, dihydrodibenzoxepinyl, dihydrodibenzothiepinyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, oxofluorenylcarbonyl, oxodihydroanthrylcarbonyl, dioxodihydroanthrylcarbonyl, furoyl, pyridylcarbonyl, chromonylcarbonyl, quinolylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, indolin-1-ylcarbonyl, dihydrodibenzazepinyl-N-carbonyl, tetrahydroquinolyl-N-carbonyl, tetrahydrobenzazepinyl-N-carbonyl, methanesulfonyl, benzenesulfonyl, p-toluenesulfonyl, naphthalenesulfonyl, quinolinesulfonyl, and diphenylphosphinoyl, where each aromatic ring system may be independently substituted with one to three substituents selected independently from the group consisting of halogen, cyano, C₁ - C₆ alkyl, trifluoromethyl, C₃ - C₈ cycloalkyl, phenyl, benzyl, hydroxy, C₁ - C₆ alkoxy (optionally partially or completely fluorinated), benzyloxy, phenoxy, mercapto, C₁ - C₆ alkylthio, carboxy, C₁ - C₆ alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, C₁ - C₆ alkylamino, and di(C₁ - C₆ alkyl)amino, or two adjacent substituents together form methylenedioxy.

51. (Withdrawn): A pharmaceutical composition comprising:

(a) at least one compound selected from the group consisting of compounds of formula I:

Application No. 09/693,558

Page 24



where:

each of $R^{1(i)}$, $R^{2(i)}$, $R^{3(i)}$, and $R^{4(i)}$ are independently selected from the group consisting of hydrogen, halogen, hydroxy, trifluoromethyl, cyano, aliphatic hydrocarbyl residue optionally substituted with one or more functional groups and optionally interrupted by one or more heteroatoms, and aromatic hydrocarbyl residue; or $R^{1(i)}$ and $R^{2(i)}$ together form a bridge;

k is 0 or 1;

$A^{(i)}$ and $D^{(i)}$ are independently a saturated or unsaturated optionally substituted aliphatic hydrocarbyl residue, optionally interrupted by a heteroatom or a functional group;

E is a bond or is a heterocyclic residue having one or two ring nitrogen atoms or one ring nitrogen atom and one ring oxygen atom, linked to $D^{(i)}$ and G through a ring nitrogen atom and a ring carbon atom or through two ring nitrogen atoms; and

G is selected from the group consisting of hydrogen, an aliphatic or araliphatic residue, an unsaturated or aromatic monocyclic or polycyclic carbocyclic residue, a saturated, unsaturated, or aromatic monocyclic or polycyclic heterocyclic residue, bonded directly or through a functional group derived from a carbon, nitrogen, oxygen, sulfur, or phosphorus atom,

and the stereoisomers or racemic or non-racemic mixtures of stereoisomers thereof,

and the tautomers thereof when G is a heterocyclic aromatic ring or an aromatic ring substituted by a hydroxy, mercapto, or amino group,

and the pharmacologically acceptable acid addition salts thereof;

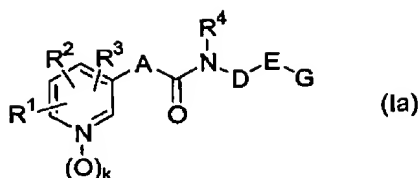
(b) a compound having vitamin PP activity or a prodrug thereof; and

(c) at least one physiologically acceptable carrier.

52. (Withdrawn): The composition of claim 41 where the compound(s) of formula I are selected from the group consisting of compounds of formula Ia:

Application No. 09/693,558

Page 25



where:

R^1 is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl, and hydroxy;

R^2 and R^3 are each hydrogen;

R^4 is hydrogen or hydroxy;

A is selected from the group consisting of ethylene, propylene, or butylene, each optionally substituted with hydroxy or one or two fluorine atoms, $-OCH_2-$, $-SCH_2-$, ethenylene, vinylene, and butadienylene;

D is selected from the group consisting of $C_2 - C_6$ alkylene and $C_2 - C_6$ alkenylene, where the double bond may also join D and E;

E is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine, and morpholine; and

G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl, furylmethyl, thienylmethyl, thiazolylmethyl, pyridylmethyl, benzothienylmethyl, quinolylmethyl, phenylthienylmethyl, phenylpyridylmethyl, dihydrodibenzoxepinyl, dihydrodibenzothiepinyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, oxofluorenylcarbonyl, oxodihydroanthrylcarbonyl, dioxodihydroanthrylcarbonyl, furoyl, pyridylcarbonyl, chromonylcarbonyl, quinolylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, indolin-1-ylcarbonyl, dihydrodibenzazepinyl-N-carbonyl, tetrahydroquinolyl-N-carbonyl, tetrahydrobenzazepinyl-N-carbonyl, methanesulfonyl, benzenesulfonyl, p-toluenesulfonyl, naphthalenesulfonyl, quinolinesulfonyl, and diphenylphosphinoyl, where each aromatic ring system may be independently substituted with one to three substituents selected independently from the group consisting of halogen, cyano, $C_1 - C_6$ alkyl, trifluoromethyl, $C_3 - C_8$ cycloalkyl, phenyl, benzyl, hydroxy, $C_1 - C_6$ alkoxy (optionally partially or completely fluorinated), benzyloxy, phenoxy, mercapto, $C_1 - C_6$

Application No. 09/693,558

Page 26

alkylthio, carboxy, C₁ - C₆ alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, C₁ - C₆ alkylamino, and di(C₁ - C₆ alkyl)amino, or two adjacent substituents together form methylenedioxy.

53. (Withdrawn): The method of claim 50 where the cancerostatic or immunosuppressive agent is selected from the group consisting of compounds of formula Ia where:

R¹ is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl, and hydroxy;

R² and R³ are each hydrogen;

R⁴ is hydrogen or hydroxy;

A is selected from the group consisting of ethylene, propylene, or butylene, each optionally substituted with hydroxy or one or two fluorine atoms, -OCH₂-, -SCH₂-, ethenylene, vinylene, and butadienylene;

D is selected from the group consisting of C₂ - C₆ alkylene and C₂ - C₆ alkenylene, where the double bond may also join D and E;

E is selected from the group consisting of pyrrolidine, piperidine, and hexahydroazepine; and

G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, methanesulfonyl, benzenesulfonyl, p-toluenesulfonyl, and naphthalenesulfonyl, where each aromatic ring system may be independently substituted with one to three substituents selected independently from the group consisting of halogen, cyano, C₁ - C₆ alkyl, trifluoromethyl, C₃ - C₈ cycloalkyl, phenyl, benzyl, hydroxy, C₁ - C₆ alkoxy (optionally partially or completely fluorinated), benzyloxy, phenoxy, mercapto, C₁ - C₆ alkylthio, carboxy, C₁ - C₆ alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, C₁ - C₆ alkylamino, and di(C₁ - C₆ alkyl)amino, or two adjacent substituents together form methylenedioxy.

54. (Withdrawn): The method of claim 53 where the cancerostatic or immunosuppressive agent is selected from the group consisting of compounds of formula Ia where:

R¹ is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl, and hydroxy;

Application No. 09/693,558

Page 27

R^2 and R^3 are each hydrogen;

R^4 is hydrogen or hydroxy;

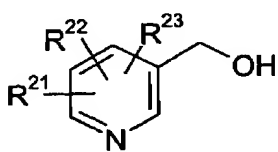
A is selected from the group consisting of ethylene, propylene, or butylene, each optionally substituted with hydroxy or one or two fluorine atoms, $-OCH_2-$, $-SCH_2-$, ethenylene, vinylene, and butadienylene;

D is selected from the group consisting of $C_2 - C_6$ alkylene and $C_2 - C_6$ alkenylene, where the double bond may also join D and E;

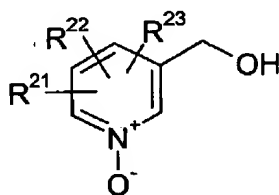
E is selected from the group consisting of pyrrolidine, piperidine, and hexahydroazepine; and

G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, and dihydrodibenzocycloheptenyl, where each aromatic ring system may be independently substituted with one to three substituents selected independently from the group consisting of halogen, cyano, $C_1 - C_6$ alkyl, trifluoromethyl, $C_3 - C_8$ cycloalkyl, phenyl, benzyl, hydroxy, $C_1 - C_6$ alkoxy (optionally partially or completely fluorinated), benzyloxy, phenoxy, mercapto, $C_1 - C_6$ alkylthio, carboxy, $C_1 - C_6$ alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, $C_1 - C_6$ alkylamino, and di($C_1 - C_6$ alkyl)amino, or two adjacent substituents together form methylenedioxy.

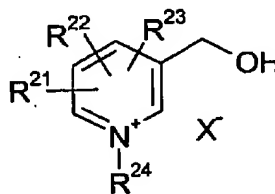
55. (Previously presented) The method of claim 32 where the compound having vitamin PP activity or a prodrug thereof is selected from the group consisting of compounds of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va, and Vb:



(II)



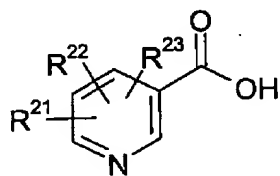
(IIa)



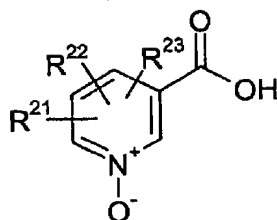
(IIb)

Application No. 09/693,558

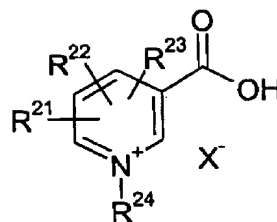
Page 28



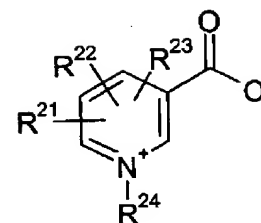
(III)



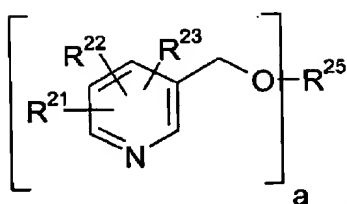
(IIIa)



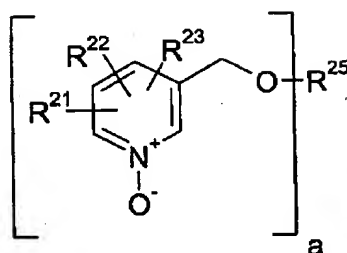
(IIIb)



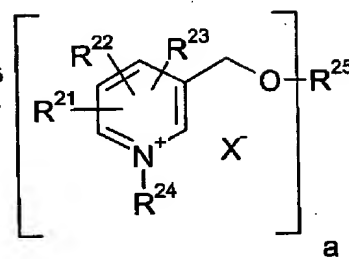
(IIIc)



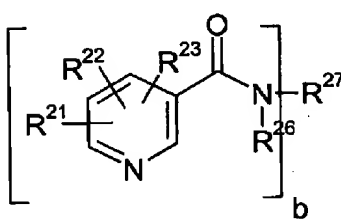
(IV)



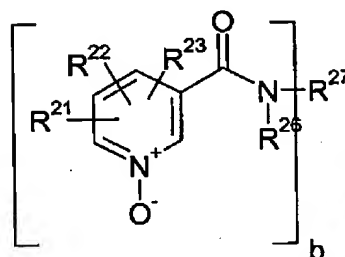
(IVa)



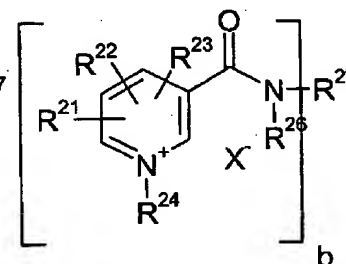
(IVb)



(V)



(Va)



(Vb)

where:

a is an integer of 1 through 6;

b is an integer of 1 through 2;

X⁻ is selected from the group consisting of fluoride, chloride, bromide, iodide, hydrogensulfate, mesylate, trifluoromethanesulfonate, tosylate, tetrafluoroborate, dihydrogenphosphate, and acetate;

R²¹ is selected from the group consisting of hydrogen, halogen, cyano, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, alkylthio, aminoalkyl, amino, alkylamino,

Application No. 09/693,558

Page 29

dialkylamino, formyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and carboxy;

R^{22} is selected from the group consisting of hydrogen, halogen, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, aminoalkyl, amino, alkoxycarbonyl, aminocarbonyl, and carboxy;

R^{23} is selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl;

R^{24} is selected from the group consisting of alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, and aralkyl;

R^{25} is the residue of an alcohol $R^{25}(OH)_a$ selected from monovalent linear and branched C_{1-10} alkanols and ω -dialkylaminoalkanol, benzyl alcohol, divalent linear and branched C_{2-10} diols, mono- or divalent C_{5-7} cycloalkanols, C_{5-7} cycloalkanediols, C_{5-7} cycloalkanemethanols, saturated C_{5-7} heterocyclomethanols, tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms, glycerin, 2,2-bis(hydroxymethyl)-1-octanol, erythritol, pentaerythritol, arabitol, xylitol, sorbitol, mannitol, isosorbitol, tetra(hydroxymethyl)cyclohexanol, and inositol;

R^{26} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

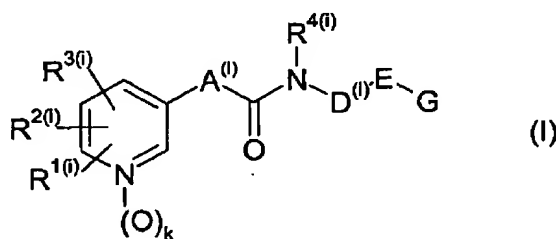
when b is 2, R^{27} is alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl;

and the C=S analogs of C=O groups,

and the acid addition salts or the sodium, potassium, magnesium, calcium or aluminum salts thereof.

56. (Withdrawn) A pharmaceutical composition comprising:

(a) at least one compound selected from the group consisting of compounds of formula I:



where:

Application No. 09/693,558

Page 30

each of $R^{1(i)}$, $R^{2(i)}$, $R^{3(i)}$, and $R^{4(i)}$ are independently selected from the group consisting of hydrogen, halogen, hydroxy, trifluoromethyl, cyano, aliphatic hydrocarbyl residue optionally substituted with one or more functional groups and optionally interrupted by one or more heteroatoms, and aromatic hydrocarbyl residue; or $R^{1(i)}$ and $R^{2(i)}$ together form a bridge;

k is 0 or 1;

$A^{(i)}$ and $D^{(i)}$ are independently a saturated or unsaturated optionally substituted aliphatic hydrocarbyl residue, optionally interrupted by a heteroatom or a functional group;

E is a bond or is a heterocyclic residue having one or two ring nitrogen atoms or one ring nitrogen atom and one ring oxygen atom, linked to $D^{(i)}$ and G through a ring nitrogen atom and a ring carbon atom or through two ring nitrogen atoms; and

G is selected from the group consisting of hydrogen, an aliphatic or araliphatic residue, an unsaturated or aromatic monocyclic or polycyclic carbocyclic residue, a saturated, unsaturated, or aromatic monocyclic or polycyclic heterocyclic residue, bonded directly or through a functional group derived from a carbon, nitrogen, oxygen, sulfur, or phosphorus atom,

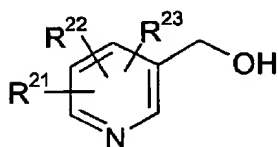
and the stereoisomers or racemic or non-racemic mixtures of stereoisomers thereof,

and the tautomers thereof when G is a heterocyclic aromatic ring or an aromatic ring

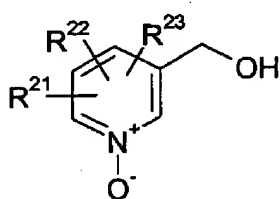
substituted by a hydroxy, mercapto, or amino group,

and the pharmacologically acceptable acid addition salts thereof;

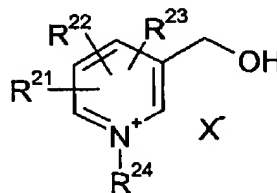
(b) at least one compound selected from the group consisting of compounds of formulae II, IIa, IIb, III, IIIa, IIIb, IIIc, IV, IVa, IVb, V, Va, and Vb:



(II)



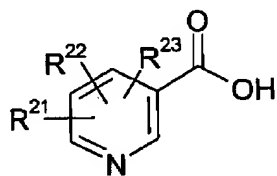
(IIa)



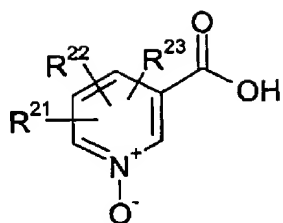
(IIb)

Application No. 09/693,558

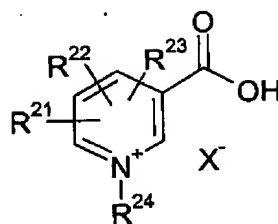
Page 31



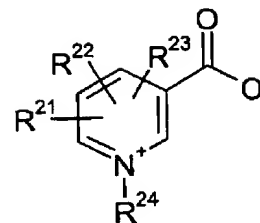
(III)



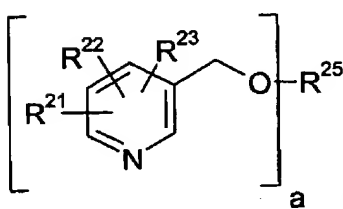
(IIIa)



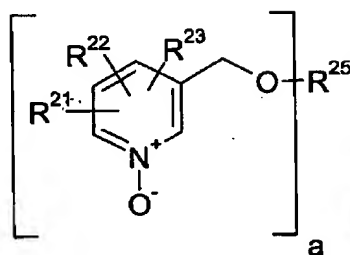
(IIIb)



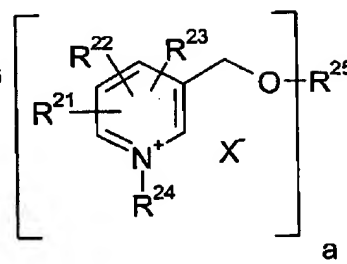
(IIIc)



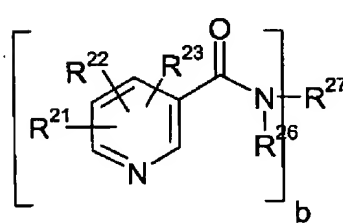
(IV)



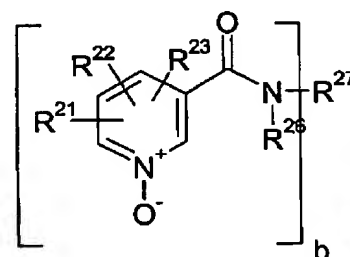
(IVa)



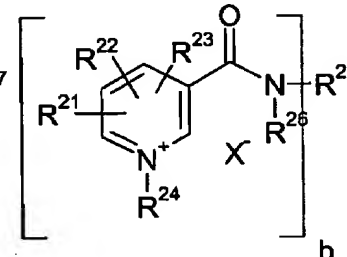
(IVb)



(V)



(Va)



(Vb)

where:

a is an integer of 1 through 6;

b is an integer of 1 through 2;

X⁻ is selected from the group consisting of fluoride, chloride, bromide, iodide, hydrogensulfate, mesylate, trifluoromethanesulfonate, tosylate, tetrafluoroborate, dihydrogenphosphate, and acetate;

R²¹ is selected from the group consisting of hydrogen, halogen, cyano, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, alkylthio, aminoalkyl, amino, alkylamino,

Application No. 09/693,558

Page 32

dialkylamino, formyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and carboxy;

R^{22} is selected from the group consisting of hydrogen, halogen, alkyl, trifluoromethyl, hydroxyalkyl, hydroxy, alkoxy, alkanoyloxy, aminoalkyl, amino, alkoxycarbonyl, aminocarbonyl, and carboxy;

R^{23} is selected from the group consisting of hydrogen, alkyl, and hydroxyalkyl;

R^{24} is selected from the group consisting of alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, and aralkyl;

R^{25} is the residue of an alcohol $R^{25}(OH)_a$ selected from monovalent linear and branched C_{1-10} alkanols and ω -dialkylaminoalkanols, benzyl alcohol, divalent linear and branched C_{2-10} diols, mono- or divalent C_{5-7} cycloalkanols, C_{5-7} cycloalkanediols, C_{5-7} cycloalkanemethanols, saturated C_{5-7} heterocyclomethanols, tri-, tetra-, penta-, and hexavalent linear, branched, and cyclic alcohols with 3 to 10 carbon atoms, glycerin, 2,2-bis(hydroxymethyl)-1-octanol, erythritol, pentaerythritol, arabitol, xylitol, sorbitol, mannitol, isosorbitol, tetra(hydroxymethyl)cyclohexanol, and inositol;

R^{26} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 1, R^{27} is selected from the group consisting of hydrogen, alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, dialkylaminoalkyl, and carboxymethyl;

when b is 2, R^{27} is alkylene in which a methylene group is optionally replaced by O, NH, or N-alkyl;

and the C=S analogs of C=O groups,

and the acid addition salts or the sodium, potassium, magnesium, calcium or aluminum salts thereof;

and

(c) at least one physiologically acceptable carrier.